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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,674	10/12/2001	Steve Oi	70669	1084

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EXAMINER	
WALICKA, MALGORZATA A	
ART UNIT	**PAPER NUMBER**
1652	8

DATE MAILED: 01/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,674	OI ET AL.	
	Examiner	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *7,14 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

The Response to Restriction Requirement filed on Nov. 4, 2003, as paper No. 7 is acknowledged. The amendments to the claims have been entered as requested. Claims 17-21 are canceled. Claims 1-16 are pending. Claims 7 and 14-15 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 7. Claims 1-6 and 8-13 are the subject of this Office Action.

Detailed Office Action

1. Objections

The oath or declaration is defective, because it misses the date of filing the utility application.

2. Restriction election

The Applicants elected, with traverse, Group I drawn to DNA encoding novel serine protease, expression vectors, recombinant host, and recombinant production of the enzyme. In response to restriction between species Applicants elected SEQ ID NO: 4 encoding SEQ ID NO: 3.

The traverse is on the ground that "With respect to Group I and II, it is herein urged that the subject matter of each group is not distinct and that there is no burden on the Office in examining the claims in these groups in a single Application." Furthermore, "Group I, claims 1-6 and 8-13, drawn to DNA encoding serine proteases and related subject matter, and Group II, claims 7, and 14-16, drawn to those serine proteases, are related as a product and DNA encoding same which is useful in making that product.

As between inventions that are related in this manner, restriction is proper if the DNA may be used to make another materially different product, or if the product may be made from a materially different DNA."

Applicants' arguments have been fully considered but are found not persuasive. Regarding the burden on the Office, although the searches of Group I and II are overlapping, they are not coextensive. Search of Group I and II would include searching of class 435, subclass 219, but searching Group I would also include class 435, subclass 320.1, and class 536, subclass 23.2, which is not necessary for the search of Group II.

Regarding relatedness of Group I and II, as indicated in the restriction requirement, paper No. 6, inventions I and II are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01).

In the instant case the different inventions DNA, and related subject, and encoded protease are divergent molecules having different chemical structures, biological functions and effects. DNA encodes the proteases, but the protease has different effect, because it cleaves another protein. Both inventions are not capable of use together.

Applicants argue that DNA may not be used "to make another materially different product." On contrary, DNA may be used to make a DNA probe or primer. Also, the

DNA may be used in methods other than production of the enzyme; for example, it can be used in hybridization assays.

In paper No. 6 the examiner required restriction between groups of inventions marked as I-IV and one of inventions (A)-(C):

(A). SEQ ID No: 2 encoding SEQ ID No: 1,

(B). SEQ ID No: 4 encoding SEQ ID No: 3, and

(C). SEQ ID No: 6 encoding DNA SEQ ID No: 5.

The election of invention (B) directed to SEQ ID No: 3 or a sequence encoding SEQ ID No: 4, is acknowledged.

This, however, is not the election of species, as Applicants assume in their response by writing "should no generic claim be allowed." SEQ ID NOs: 1-3, and respective DNA molecules, belong to the genus of dipeptidyl peptidase IV–related proteins (DPRP), orto the genus of respective encoding DNA molecules, however, the chemical structure of each of these proteases is different and one skilled in the art, having in hand the structure of one representative of the genus is unable predict the amino acid sequence of the other species. Hence, the species being different chemical compounds are independent inventions.

In conclusion, although Applicant's arguments are fully considered they are found not persuasive. Applicants are kindly reminded that restriction involves four factors: burden on the examiner, distinctness, independence and classification. The restriction, as requested in the paper No. 6, includes all these factors, thus it is proper and made FINAL.

3. Rejections

3.1. 35 USC section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.1.1. Lack of written description

Claims 1-6 and 8-13 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amino acid sequence of SEQ ID NO: 3 is referred to in Table I, and on page 8, line 5 of the specification, as consisting of 864 amino acids. The paper sequence listing, however, identifies SEQ ID NO: 3 as consisting of 863 amino acids. As such, the presence of amino acid residue No. 864 of the claimed DPRP-2 protease variant of SEQ ID NO: 3 is unclear.

Claims 1, 2, 6, 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims are directed

to an alternative splice variant of DPRP-2 having DNA SEQ ID NO: 4. The claims are directed to a genus of splice variants for which there is no predictability of structure and function, because each splice variant has its unique structure and may have a unique function. Some splice variants may retain their dipeptidase function, some may be inactive and some may gain a new function. On page 9, line 34, Applicants teach that DPRP-2 is encoded by a gene that has 27 exons. Theoretically, the gene has 25 introns. Thus, theoretically, the maximal number of splice variants that may origin from a gene having 25 introns is 2^{25}, i.e., 3.35 $x10^{7}$. The specification discloses only nine splice variants of DPRP-2, having protein sequences set forth by SEQ ID NOs: 3, 23, 25, 27, 29, 31, 33, 35, 37 and 39 that are encoded by DNA sequences set forth by SEQ ID NOs: 4, 24, 26, 28, 30, 34, 36, 38 and 40. A person skilled in the art recognizes that in the particular case of splice variants, none of the variants, or even tens of them, does not characterize the structure and function of the genus, because one cannot establish only one function/structure relationship for the genus and thus the presence of a large number of species is still deemed to be not representative of the genus. Therefore, any claimed splice variant of the DPRP-2 is sufficiently described only when its structure is recited by the claim.

In summary, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

3.1.2. Scope of eneblement

Claims 1, 2, 6, 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for splice variants of DPRP-2 that are encoded by

DNA sequences set forth by SEQ ID NOs: 4, 24, 26, 28, 30, 34, 36, 38 and 40, does not reasonably provide enablement for any splice variant of DPRP-2 or complement thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are broader than the enablement provided by the disclosure with regard to the extremely large number of DNA molecules, theoretically about 3.35 $x10^7$, which are encompassed by them.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Otherwise, undue experimentation is necessary to make the claimed invention. Factors to be considered in determining whether undue experimentation is required, are summarized *In re* Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the nature of the invention, (b) the breadth of the claim, (c) the state of the prior art, (d) the relative skill of those in the art, (e) the predictability of the art, (f) the presence or absence of working example, (g) the amount of direction or guidance presented, (h) the quantity of experimentation necessary.

The nature and breath of the claimed invention encompasses any DNA molecule comprising a sequence that includes any alternative splice variant of SEQ ID NO: 4 or a complement thereof.

While methods of gene cloning, sequencing, as well as synthesizing and modifying, are well known in the relevant art, and skills of the artisans highly developed,

identifying in biologic or man-made sources, or producing, any of about 3.35 $x10^7$ splice variants or the complements thereof is outside the realm of routine experimentation. In addition, the probability of success in obtaining the claimed invention is low.

The examples provided by the disclosure are SEQ ID NOs: 4, 24, 26, 28, 30, 34, 36, 38 and 40 splice variant of DPRP-2. The specification fails to disclose all splice variant of SEQ ID NO; 4, i.e. splice variant of DPRP-2, neither the specification teach how to modify SEQ ID NOs: 4 to obtain such variants. Applicants' enablement is limited to SEQ ID NOs: 4, 24, 26, 28, 30, 34, 36, 38 and 40. Thus, Applicants did not provide sufficient guidance how to make the claimed invention. Without the further guidance on the part of Applicants as to the structure of splice variants of DPRP-2 the experimentation left to those in the art is improperly extensive and undue.

3.2. 35 USC section 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1, 2, 6, 8, 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Lamerdin, J. E. et al. (1998) who disclosed two polypeptides with more than 90% similarity to SEQ ID NO: 3 of the instant application, having annotated function of prolyl oligopeptidase; see the enclosed sequence alignment. The DNA molecules encoding

both polypeptides are located on chromosome 19, as is DNA of SEQ ID NO: 4 of the instant application. The accession numbers for said polypeptides are:

1) AAC33801 for the polypeptide consisting of 508 amino acids (91.7% similarity to SEQ ID NO: 3), encoded by nucleotides 1-1524 of the polynucleotide with accession No. AC005594.1, and

2) AAC62840.1 for the polypeptide consisting of 432 amino acids (97.52% similarity to SEQ ID NO: 3 of the instant application), encoded by nucleotides 1-1293 of the polynucleotide with accession No. AC0062840.1; see the enclosed prints of sequences from PubMed.

The sequences disclosed by Lamerdin et al. are isolated nucleic acid which encode additional splice variants of the prolyl dipeptidase disclosed in this application as DPRP-2.

4. Conclusion

No claim is allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner

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